A copy of the claims as pending after entry of the foregoing amendment is attached hereto as Appendix A. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

The Rejections Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the relevant art to make and/or use the invention. Applicants believe the rejection should be withdrawn for the reasons stated below.

The Examiner alleges that the instant specification does not provide adequate teaching and guidance to prevent one of skill in the art from participating in undue experimentation in order to use the claimed invention. Because the claimed gro-1 is a human homolog, the Examiner believes that the "use" of gro-1 of SEQ ID NO:3 "on" multicellular vertebrates cannot be predicted based on the function of *C. elegans* gro-1 (see Office Action mailed October 2, 2002 on page 3, lines 15-19). Applicants point out that the pending claims are not directed to methods of use but rather nucleic acid compositions. Applicants clearly disclosed the sequences of the human gro-1 homolog in the present specification therefore one of skill in the art can easily make the claimed invention.

The Examiner alleges that, although both human and *C. elegans* gro-1 polypeptides are tRNA isopentenyl transferases, the effect on the growth and physiology in humans cannot be predicted. Applicants invite the Examiner's attention to Golovko et al. (2000, *Gene* 258:85-93; previously submitted as Exhibit II with the Amendment filed June 15, 2001). Human gro-1 was shown to complement yeast that was mutant for the gro-1 homologue, named mod-5. This indicates that functionally human gro-1 does have isopentenyl transferase enzymatic activity. As such, there is no reason to assume that human gro-1 does not possess that activity in humans. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *In re Marzocchi,* 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971); *In re Brana,* 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). Without undue experimentation, one of skill in the art can use the nucleic acids of the invention to monitor expression levels or localization of the enzyme. Undue experimentation is experimentation that would require

a level of ingenuity *beyond* what is expected from one of ordinary skill in the field. *Fields v. Conover,* 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971).

The Examiner further alleges that, while the specification does enable a method for screening for functional fragments of *C. elegans* gro-1 based on rescue of mutant phenotypes, functional fragments of human gro-1 are not enabled. Applicants respectfully disagree.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics, Inc.* 857 F.2d 778, 8 USPQ 2d 1217 (Fed. Cir. 1988). Enablement is not precluded even if some experimentation is necessary *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986). The need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112. This is so even if the amount of experimentation required is laborious. *In re Wands* 858 F.2d 731 (Fed. Cir. 1988).

In the present case, the level of skill in the art at the time of filing included *C. elegans* rescue assays where cDNAs from non-*C. elegans* species were introduced into mutant nematodes to rescue mutant phenotypes. This technology was in use by 1993, see for example, Stern et al (1993, *Mol. Biol. Cell* 4:1175-88; Reference BL submitted herewith) rescued a sem-5 mutant *C. elegans* with the addition of a human or *Drosophila* homologue (GRB2 or Drk respectively). Proper cell signaling was restored by the ability of the non-*C. elegans* proteins to functionally replace the mutant sem-5. Additionally, Levitan et al. (1996, *PNAS* 93:14940-4; Reference BM submitted herewith) demonstrated that human presenilin nucleic acids could rescue the egg laying defect of SEL-12 mutant *C. elegans*. This is particularly interesting when considering the apparently disparate physiological functions of the human and nematode polypeptides. Although presenilin is a human protein with involvement in Alzheimer's disease, Levitan et al. experimented with rescuing an egg laying defect in *C. elegans* based on a mere 50% homology between the two proteins. The successful rescue indicates that even proteins with a weak similarity (as the Examiner alleges for the human and *C. elegans* gro-1 homologues) can be used in this method. Thus, one of

skill in the art would be able to screen for functionally active human gro-1 fragments by rescuing mutant *C. elegans* without undue experimentation.

In view of the foregoing, Applicants request that the Examiner withdraws the rejections under 35 U.S.C. §112, first paragraph.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: February 3, 2003

By: Laura A Coruzzi 40,258

30,742

Laura A. Coruzzi (Reg. No.)
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090